In the Specification

Please amend the specification as follows. Replacement paragraphs are presented with insertions indicated by underlining (except for existing underlining, e.g., which indicates genus and species, such as Thermotoga Maritima) and deletions indicated by strikethrough.

Please replace the paragraph beginning on page 11, line 1 with the following paragraph:

Further, the present invention relates to the method in which the RRF protein crystal is characterized by a structure coordinate described in ~~Table 7~~ Table 8.

Please replace the paragraph beginning on page 13, line 11 with the following paragraph:

Further, the present invention relates to the method in which the structure coordinate is a structure coordinate of the RRF protein according to ~~Table 7~~ Table 8.

Please replace the paragraph beginning on page 16, line 4 with the following paragraph:

Further, the present invention relates to the RRF protein crystal characterized by a structure coordinate according to ~~Table 7~~ Table 8.

Please replace the paragraph beginning on page 26, line 9 with the following paragraph:

"Heavy atom derivative" refers to a chemically modified form of RRF protein crystal. In making it, in actuality, the crystal is dipped in a solution containing a heavy metal atom salt or an organometal compound that can diffuse through the crystal and bind to the surface of a protein (for example, lead chloride, gold thiomaleate, thyromethal or uranyl acetate). The position or positions of bound heavy metal atom or atoms can be determined by X-ray diffraction analysis of the dipped crystal. Then, using the data, phase data used for constructing the three-dimensional

structure of an enzyme are prepared. One skilled in the art will understand that the set of structure coordinate determined by X-ray crystallography has a standard error. For the purpose of the present invention, any set of structure coordinates of RRF, RRF homologue or RRF mutant having a root-mean-square value deviation of protein backbone atoms (N, Cα, C and 0) of less than 0.75Å when superposed on the structure coordinates enumerated in ~~Table 7~~ Table 8 should be considered the same.

Please replace the paragraph beginning on page 27, line 15 with the following paragraph:

"Molecular substitution" refers to a method including a step of orienting and positioning another molecule whose structure coordinates (for example, the structure coordinates shown in ~~Table 7~~ Table 8) are known in the unit lattice of an unknown crystal to thereby prepare a provisional model of RRF crystal whose structure coordinates are unknown such that the observed diffractive pattern of the unknown crystal can be optimally explained. Then, a phase is calculated based on this model and synthesized with the observed amplitude to obtain an approximate Fourier synthesis of the structure whose coordinates are unknown. Then, application to a purified substance enables one to finally obtain an accurate structure of the unknown crystal. By use of the structure coordinates of RRF of the present invention and by use of molecular substitution, the structure coordinates of a mutant, homologue, or co-complex or different crystal structure of RRF can be determined.

Please replace the paragraph beginning on page 29, line 10 with the following paragraph:

The present invention provides for the first time the crystals of RRF of strain X and of Thermotoga Maritima RRF and the structures of RRF determined therefrom. On the other hand, the crystal of Thermotoga Maritima RRF was formed from an ammonium sulfate solution. The crystal has space group P43212 of a bipyramid type. The unit lattice of the crystal has a=b=47.3Å, c=297.6Å. The structure coordinate of RRF is shown in ~~Table 7~~ Table 8. The crystal packing indicates that RRF is a monomer.

Please replace the paragraph beginning on page 34, line 13 with the following paragraph:

One of the methods that can be used for this purpose is molecular substitution. In this method, whether or not an unknown crystal structure is the crystal form of another form of RRF, RRF mutant or RRF co-complex or any other optional protein having an amino acid sequence that is significantly homologous to any optional functional domain of RRF can be determined by use of the structure coordinate of RRF of the present invention as provided in ~~Table 7~~ Table 8. This method provides accurate structural form about an unknown crystal more quickly and efficiently than trying to determine such data from the beginning.

Please replace the paragraph beginning on page 39, line 4 with the following paragraph:

There may be used one of methods of screening the chemical bodies or fragments on their ability of binding to respective binding pockets of RRF, more particularly the binding site or accessory binding site of the RRF, or to other pockets not participating in binding to the substrate or the like upon expression of the activity of the RRF. This process can be started by visual study of the active site, for example, upon computer screening based on the RRF coordinate in ~~Table 7~~ Table 8. For example, as shown in the sketch by a ribbon in Fig. 3, the RRF that has a form of "L"-shape has a pocket in the vicinity of C-terminal positioned at the "L"-shaped bent portion that separates the two domains. A compound bound to the pocket can be a leading candidate of an inhibitory compound to the RRF. The above-mentioned pocket can be readily observed by preparing a space-packing model based on the RRF coordinate shown in ~~Table 7~~ Table 8 by use of a software of Rasmol et al. The pocket is positioned between the two domains of the RRF and hence, it suggested the possibility that it participates in the activity of the RRF through adjustment of the angle between the domains. Then, the selected fragment or chemical entity can be positioned in various orientations or can couple to the respective binding pockets of the RRF. The coupling can be achieved by use of software such as Quanta and Sybyl

and thereafter, minimization of energy and molecular kinetics are performed by use of a standard molecular mechanism force field (for example, CHARMM, AMBER).

Please replace Table 1 beginning on page 60, line 11 with the following Table. Please note that the word "Average" has not been inserted – it was underlined in Table 1 as filed:

Table 1

Lower limit and upper limit of shell		Diffraction intensity		Average	Normal	Linear multiplier	Quadratic multiplier
Angstrom		Average	Error	Stat. value	$\chi 2$ value	R-factor	R-factor
Lower limit	Upper limit						
30.0	7.12	814.6	36.6	18.5	0.709	0.033	0.032
7.12	5.67	227.1	16.7	13.5	1.012	0.084	0.072
5.67	4.95	266.0	19.0	15.3	0.983	0.083	0.075
4.95	4.50	417.3	25.3	18.4	1.052	0.070	0.064
4.50	4.18	394.0	25.5	19.6	1.239	0.087	0.086
4.18	3.93	330.4	24.4	19.7	1.064	0.093	0.088
3.93	3.74	296.1	24.6	20.9	1.286	0.125	0.219
3.74	3. 58	283.8	25.5	22.0	1.275	0.142	0.221
3.58	3.44	207.5	23.2	21.2	1.314	0.170	0.192
3.44	3.32	173.2	22.5	21.1	1.278	0.193	0.298
3.32	3.22	151.8	22.1	20.9	1.414	0.222	0.231
3.22	3.12	130.4	21.7	20.8	1.560	0.265	0.280
3.12	~~3.01~~ 3.04	108.3	20.6	19.9	1.552	0.306	0.307
3.04	2.97	92.2	19.9	19.2	1.655	0.334	0.315
2.97	2.90	74.9	19.2	18.7	1.632	0.411	0.416
Total reflection		268.4	23.2	19.3	1.259	0.119	0.102

Please replace the paragraph beginning on page 80, line 7 with the following paragraph:

There may be used one of methods of screening the chemical bodies or fragments on their ability of binding to respective binding pockets of RRF, more particularly the binding site or accessory binding site of the RRF, or to other pockets not participating in binding to the substrate or the like upon expression of the activity of the RRF. This process can be started by visual study of the active site, for example, upon computer screening based on the RRF coordinate in ~~Table 7~~ Table 8. For example, as shown in the sketch by a ribbon in Fig. 3, the RRF that has a form of "L"-shape has a pocket in the vicinity of C-terminal positioned at the "L"-shaped bent portion that separates the two domains. A compound bound to the pocket can be a leading candidate of an inhibitory compound to the RRF. The above-mentioned pocket can be readily observed by preparing a space-packing model based on the RRF coordinate shown in ~~Table 7~~ Table 8 by use of a software of Rasmol et al. The pocket is positioned between the two domains of the RRF and hence, it suggested the possibility that it participates in the activity of the RRF through adjustment of the angle between the domains. Then, the selected fragment or chemical entity can be positioned in various orientations or can couple to the respective binding pockets of the RRF. The coupling can be achieved by use of software such as Quanta and Sybyl and thereafter, minimization of energy and molecular kinetics are performed by use of a standard molecular mechanism force field (for example, CHARMM, AMBER).

Please replace the paragraph beginning on page 93, line 2 with the following paragraph:

Structure coordinates ~~cooedinates~~ of RRF